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LICATLA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
CELSA, BENNETT M	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,054	LU, ZHE	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 9-14* is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/4/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-14 are currently pending.

Claims 1 and 5-8 are under consideration.

Claims 2-4 and 9-14 are withdrawn from further consideration as being drawn to a nonelected invention.

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1, 7 and 8) in Paper Correspondence dated July 7, 2004 is acknowledged.

2. The traversal is on the ground(s) that all the claims are linked to form a single general inventive concept under PCT Rule 13.1 since the "claims ... relate to the concept of inhibiting activity of inward-rectifier potassium channels using the tertiapin-like alpha helix compounds of the present invention". This is not found persuasive because "tertiapin-like alpha helix compounds" were known in the art (e.g. see Hider reference) and thus can not serve as a "special" technical feature to link the composition to its method of use. Additionally, the office action further provides a rationale as to the why the various methods fail to share a special technical feature e.g. address different objectives and/or utilize different protocols and method steps.

Applicant argues that "patentability over prior art should not be considered for the question of restriction".

This argument was considered but deemed nonpersuasive since the present application was filed as a national (e.g. 35 USC 371) application claiming priority to

PCT/US99/15308 which renders lack of unity rules applicable to the present application. Accordingly, PCT Rules 13.1 and 13.2 require that a common feature linking a composition to its method represent a "special technical feature" wherein a "technical feature" is "special" only if it represents a patentable technical feature.

Applicant further argues that "a search of the literature relating to compositions having a tertiapin-like alpha helix would clearly reveal art relating to all of these groups".

This argument was considered but deemed nonpersuasive since the restriction was not based on search considerations but was based on lack of unity, which does not require a search burden to be demonstrated. In any event, the prior office action did indicate that searching the various groups would necessitate separately burdensome manual/computer bibliographic searches in patent and literature databases.

Applicant further argues that "In the event that the Examiner will not withdraw the restriction between all of the groups in its entirety, Applicant respectfully requests that Group I be amended to include claims 5, 6, 8-12 as discussed above.

This argument was considered but deemed partially persuasive. The Examiner will consider applicant's argument as a request for "rejoinder" of claims 5, 6 and **9**-12 (since claim 8 is already part of Group I) which will be addressed below .
The requirement is still deemed proper and is therefore made FINAL.

Rejoinder Practice

> The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of

right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Pursuant to applicant's request for the rejoinder of claims 5, 6 and 9-12, the following applies.

3. Claim 1 is directed to an allowable product. Pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claims 5 and 6, directed to the process of making or using the patentable product are now subject to being rejoined. Process claims 5 and 6 are hereby rejoined and fully examined for patentability under 37 CFR 1.104. In accordance with the Official Gazette notice, *supra*, process claims 9-12, which not depend from or otherwise include all the limitations of the allowable product, NOT been rejoined.

4. Accordingly, claims 1 and 5-8 are under consideration. Claims 2-4 and 9-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Allowable Subject Matter

5. Claim 1 is allowable over the prior art of record. The prior art of record fails to disclose or suggest peptides comprising seq. Id. 2.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The methods of claims 5 and 6 are indefinite since it is unclear what "activity of inward-rectifier potassium channels" in the assay is necessary to practice the claimed methods. As such the methods fail to apprise one of ordinary skill in the art as to what activities (e.g. to be inhibited/measured etc.) would infringe or not infringe the presently claimed method.

B. In claim 7 (and claim 8, dependent thereon), the phrase "a compound having a tertiapin-like α helix" is indefinite.

Regarding the definition of the term "a compound having a tertiapin-like α helix" the specification is completely open-ended as to the scope of this term asserting an expected function resulting from a broad structural definition e.g.

A. Structural: "[B]y 'tertiapin-like α helix' it is meant a helix having a **similar** amino acid sequence and amino acid composition to P11 **or** H12 through K21 of tertiapin" with "**[S]ome variations** to the amino acid sequence and/or composition between P11 through K21 of tertiapin are expected to result in compounds of similar activity."

B. Functional : "**it is expected** that test compounds having a tertiapin-like α helix will also be effective inhibitors of inward-rectifier potassium channels".

Accordingly, the specification fails to provide a *concrete* definition as to what parameters e.g. structural (e.g. requisite peptide structure), conformational (e.g. 3 dimensional) and/or functional features (e.g. receptor binding parameters and/or helicity degree etc.) must be present in a compound such that that compound possesses "a tertiapin-like α helix" within the scope of the presently claimed invention. Additionally, the term "tertiapin-like α helix" is a relative term which renders the claim indefinite since the specification fails to provide a standard for ascertaining the requisite degree (e.g. an amount or degree of likeness to a given parameter), and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

9. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (lack of written description) .

The present claims are directed to a pharmaceutical composition comprising a "compound having a tertiapin-like α helix" and a pharmaceutically acceptable vehicle.

Regarding the definition of the term "a compound having a tertiapin-like α helix" the specification is completely open-ended as to the scope of this term asserting an expected function resulting from a broad structural definition e.g.

A. Structural: "[B]y 'tertiapin-like α helix' it is meant a helix having a **similar** amino acid sequence and amino acid composition to P11 **or** H12 through K21 of tertiapin" with "**[S]ome variations** to the amino acid sequence and/or composition between P11 through K21 of tertiapin are expected to result in compounds of similar activity."

B. Functional : "**it is expected** that test compounds having a tertiapin-like α helix will also be effective inhibitors of inward-rectifier potassium channels".

Accordingly, the specification fails to provide a concrete definition as to what parameters e.g. structural (e.g. requisite peptide structure), conformational (e.g. 3 dimensional) and/or functional features (e.g. receptor binding parameters and/or helicity degree etc.) must be present in a compound such that that compound possesses "a tertiapin-like α helix" within the scope of the presently claimed invention. Additionally, the term "tertiapin-like α helix" is a relative term in which the specification fails to provide a standard for ascertaining the requisite degree (e.g. an amount or degree of likeness to a given parameter), and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The specification examples teach that out of fourteen (14) substitute analogue derivatives of tertiapin (21 amino acid peptide) at position 13 (glutamine (Gln)) only one peptide which substitutes Met for Gln at position 13 (e.g. (M13)tertiapin) binds to inward rectifier potassium channels (e.g. GIRK1/4; ROMK1) with a Ki value very similar to that of native TPN. See also Jin et al., Biochemistry Vol. 38 (10/8/99) pages 14286-14293.

Accordingly, the present claims encompass a "generic" of compounds which:

a. Include both peptides and non-peptides;

b. Lack any core structure (peptide or non-peptide) necessary to elicit the desired activity (e.g. a tertiapin-like alpha helix), in which the features necessary to achieve the desired activity is neither defined nor adequately described by either the specification or the presently claimed invention.

c. With regard, to the ability to bind inward rectifier potassium channels (e.g. GIRK1/4; ROMK1) with a Ki value very similar to that of native TPN; there is only one (1) peptide species which supports a peptide "generic" of tertiapin position 13 substitution analogues that obtains a Ki value very similar to that of native TPN; defining a criticalily regarding position 13 for native Gln or the substitued Met at this position.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d

1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Additionally, it is noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound or a generic of compounds; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the compound or generic(s). In this regard, applicant is further referred to *University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997); "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001); and Univ. Of Rochester v G. D. Searle and Co. 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) publication pending.

Additionally, Lilly sets forth a two part test for written description:

A description of a genus of cDNA's may be achieved by means of a recitation of:

a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus Or

of a recitation of structural features common to the members of the genus.

See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

In the present instance, the claimed generic encompassing "compound(s) having a tertiapin-like α helix" is devoid of any core peptide or non-peptide chemical structure necessary to produce the desired conformational effect. Additionally this deficiency is equally true regarding the ability to mimic receptor binding action of tertiapin.

Accordingly, the specification single peptide example is not representative of the claimed genus of peptides or non-peptide which which possess a tertiapin-like α helix.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application

being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Vick US Pat.No. 3,878,297 (4/75) in view of Hider et al. Biochim. Et Biophys. Acta Vol. 667 (1981) pages 197-208 pages 197-208 alone or if necessary further in view of "Biosequence Searching For The USPO" (STN International, May 1996) pages 30-31 (hereinafter the STN manual); both Hider and STN manual cited in order to demonstrate inherency .

Claim 7 is drawn to a pharmaceutical composition comprising

a. "a compound having a tertiapin-like alpha helix"; and

b. A pharmaceutically acceptable vehicle.

Vick '297 discloses and claims a pharmaceutical composition comprising

a. apamin; and

b. A pharmaceutically acceptable vehicle.

Apamin is *inherently* "a compound having a tertiapin-like alpha helix" since:

A. Apamin is taught by the Hider reference to be "a compound having a tertiapin-like alpha helix" since Apamin is taught to possess alpha helical stucture which is similar to that of tertiapin and thus is "tertipin-like" (e.g. see pages 205-207); and/or

B. Apamin is within the scope of the specification definition of "a compound having a tertiapin-like alpa helix" e.g. "[B]y 'tertiapin-like α helix' it is meant a helix having a **similar** amino acid sequence and amino acid composition to P11 **or** H12 through K21 of tertiapin" with "**[S]ome variations** to the amino acid sequence and/or composition

between P11 through K21 of tertiapin are expected to result in compounds of similar activity." In this regard, the Hider reference in Fig. 3 aligns the Apamin and Tertiapin sequences. This alignment demonstrates that Apamin possess "similar amino sequence and amino acid composition to positions P11 or P12 (especially P12) to K21 of tertiapin" (e.g. share similarities with variations including basic amino acid (lysine or K vs. Arginine or R differences). However, the substitution of one basic hydrophilic amino acid (e.g. Arg) for another (e.g. Lys) is an art-recognized conservative substitution. See STN manual. Additionally, the Hider reference (page 205, right column) teaches the sequence similarity among all of the peptides, especially apamin and MCD peptide, in the alpha-helical region (e.g. residues 13-19) as compared to Tertiapin.

12. Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Habermann (1972) Science Vol. 177 pages 314-322 in view of Hider et al. Biochim. Et Biophys. Acta Vol. 667 (1981) pages 197-208 pages 197-208 alone or if necessary further in view of "Biosequence Searching For The USPO" (STN International, May 1996) pages 30-31 (hereinafter the STN manual); both Hider and STN manual cited in order to demonstrate inherency .

Claim 7 is drawn to a pharmaceutical composition comprising

a. "a compound having a tertiapin-like alpha helix"; and

b. A pharmaceutically acceptable vehicle.

Habermann teaches the chemical structure and pharmacological properties of pharmaceutical compositions comprising

a. apamin and mast cell degranulating peptide (MCD peptide); and

b. a pharmaceutically acceptable vehicle.

Both apamin and MCD peptide are *inherently* "compounds having a tertiapin-like alpha helix" since:

A. Both apamin and MCD peptide are taught by the Hider reference to be "a compound having a tertiapin-like alpha helix" since apamin and MCD peptide are taught to possess alpha helical stucture which is similar to that of tertiapin and thus is "tertiapin-like" (e.g. see pages 205-207); and/or

B. Both apamin and MCD peptide are within the scope of the specification definition of "a compound having a tertiapin-like alpa helix" e.g. "[B]y 'tertiapin-like α helix' it is meant a helix having a **similar** amino acid sequence and amino acid composition to P11 **or** H12 through K21 of tertiapin" with "**[S]ome variations** to the amino acid sequence and/or composition between P11 through K21 of tertiapin are expected to result in compounds of similar activity." In this regard, the Hider reference in Fig. 3 aligns Apamin and MCD peptide with the Tertiapin sequence. This alignment demonstrates that both apamin and MCD peptide possess "similar amino sequence and amino acid composition to positions P11 or P12 (especially P12) to K21 of tertiapin" e.g. with variations occuring between basic amino acids (lysine or K vs. Arginine or R). However, the substitution of one basic hydrophilic amino acid (e.g. Arg) for another (e.g. Lys) is an art-recognized conservative substitution. See STN manual. Additionally, the Hider reference (page 205, right column) teaches the sequence similarity among all of the peptides, especially apamin and MCD peptide, in the alpha-helical region (e.g. residues 13-19) as compared to Tertiapin.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-273-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
August 20, 2004